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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Application No: 09/890,829
Filing Date: 08/06/2001
First Named Inventor:Marians
Group Art Unit:
Examiner Name:
Attorney Docket No.:MSK.P-041

Examiner's Initials	US Patent Document	Name of Patentee or applicant of cited document	Date of Publication of Cited Document	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
	5,563,026	O'Donnell	10-12-1996	
	5,668,004	O'Donnell	10-09-1997	

FOREIGN PATENT DOCUMENTS

Examiner's Initials	Cite No.	office	Number	Kind Code	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document	Pages where relevant passages appear	T*

Examiner's Initials	OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS
	JANNIERE, et al., Replication terminus for DNA polymerase I during initiation of pAMbeta1 replication: role of theplasmid-encoded resolution system. Molecular microbiology. 1997, Vol. 23, No. 3, 525-535, especially pages 525-527 and 533.
	MCGLYNN et al. The DNA replication protein PriA and the recombination protein RecG bind D-loops. J. Mol. Biol. q1997, Vol. 270, pp 21`2-221, especially pages 212-214 and 217-220.
	KARET et al. Quantification of mRNA in human tissue using fluorescent nested reverse-transcriptase polymerase chain reaction. Anal. Biochem. 1994, Vol. 220, pp 384-390, especially pages 385 and 386.
	MASAI, et al. Escherichia coli PriA protein is essential for inducible and constitutive stable DNA replication, EMBO J. 1994, Vol. 13, No. 22, Page 5338-5345, especially pages 5338, 5339, 5344 and 5345.
	AL-DEIB et al. Modulation of recombination and DNA repair by the recG and PriA helicases of Escherchia cili K-12. J. Bacteriol. December 1996, Vol. 178, No. 23, pp 6782-6789, see entire document.
	MARIANS, At the Crossroads between DNA Replication and Recombination", Ray Wu Symposium, 8/15/1998.
	MARIANS, et al., Pria and the Intersection between DNA Replication and Recombination.
	SEUFERT, et al., Initiation of *Escherichia coli* minichromosome replication at *ori*C and at protein n' recognition sites. Two modes for initiating DNA synthesis *in vitro*. The EMBO Journal vol. 5, no 12, pp 3401-3406, 1986.
	JONES, et al., The ϕX174-type primosome promotes repliisome assembly at the site of recombination in bacteriophage Mu transposition, The EMBO Journal Vol. 16 No. 22, pp 6886-6895, 1997.
	ASAI, et al, D-Loops and R-Loops: Alaternative Mechanisms for the initiation of Chromosome Replication in *Escherichia coli*, Journal of Bacteriology, Apr. 1994, p. 1807-1812, Vol. 176, No. 7.
	DEVLIN, Textbook of Biochemistry with Clinical Correlations, 3rd Ed., 1992.

This Information Disclosure Citation List is being submitted as a substitute for Form PTO-1449. The Examiner is requested to place his or her initials on the lines adjacent to the citations to indicate that the reference has been considered. The Examiner is further requested to fill in his or her name and the date the information was considered in blocks at the bottom of this substitute for Form PTO-1449.

Examiner _____ **Date Considered** 1/25/2003

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/04445

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C12Q 1/68; C12P 19/34; C12N 9/00
US CL :435/6, 91.1, 91.32, 183
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 91.1, 91.32, 183, 7.32; 436/94; 536/23.1, 23.7, 23.72, 24.3, 24.33, 25.3

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

STN and WEST
D-loop, DNA replication, pri A, replisome, helicase, primosome, primosomal proteins

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JANNIERE et al. Replication terminus for DNA polymerase I during initiation of pAMbeta1 replication: role of the plasmid-encoded resolution system. Molecular Microbiology. 1997, Vol. 23, No.3, 525-535, page 525-535, especially pages 525-527 and 533.	1-4 and 14
Y	MCGLYNN et al. The DNA replication protein PriA and the recombination protein RecG bind D-loops. J. Mol. Biol. 1997, Vol. 270, Pages 212-221, especially pages 212-214 and 217-220.	1-4, 6, 7, 10 and 14

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 06 APRIL 2000	Date of mailing of the international search report 26 APR 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer FRANK LU Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet) (July 1998)★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/04445

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KARET et al. Quantification of mRNA in human tissue using fluorescent nested reverse-transcriptase polymerase chain reaction. Anal. Biochem. 1994, Vol. 220, page 384-390, especially pages 385 and 386.	1-10 and 12-14
Y	MASAI et al., Escherichia coli PriA protein is essential for inducible and constitutive stable DNA replication. EMBO J. 1994, Vol.13, No. 22, Page 5338-5345, especially pages 5338, 5339, 5344 and 5345.	1-4, 6, 7, 10 and 14
Y	AL-DEIB et al. Modulation of recombination and DNA repair by the recG and PriA helicases of Escherchia cili K-12. J. Bacteriol. December 1996, Vol. 178, No. 23, page 6782-6789, see entire document.	1-4, 6, 7, 10, 11, 14 and 15

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/04445

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	5-15	YES
	Claims	1-4	NO
Inventive Step (IS)	Claims	6-15	YES
	Claims	1-5	NO
Industrial Applicability (IA)	Claims	1-15	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-4 lack novelty under PCT Article 33(2) as being anticipated by Janniere et al., (Mol. Microbiology 23, 525-535, 1997).

Janniere et al., teach replication terminus for DNA polymerase I during initiation of pAMbeta1 replication. Replication of plasmid pAM beta 1 is initiated by DNA polymerase I (Pol I) and completed by DNA polymerase III holoenzyme contained in the replisome machinery. In this study they reported that initiation of DNA replication generates D-loop structures containing the nascent leading strand paired to its template (page 525, abstract) in a double stranded form and the displaced strand is in the single-stranded form (page 526, right column, third paragraph). The oligonucleotides used to characterize the segments extruded from D-loop replication intermediates have a length of from 20 to 50 bases (page 533, left column, second paragraph). The reaction involving Pol III HE was performed in the presence of ATP and four deoxynucleotides (page 533,right column) . This prior art meets the limitations of the claims 1-4.

Response to Arguments

In page 2, third and fourth paragraphs of applicant's Response to Written Opinion, applicant argued that: (1)" Janniere does not disclose a replication system using proteins which are added by man to a developing D-loop. Indeed, Janniere disclose no use for the purified proteins. Furthermore, no real world application of the observation of the replication intermediates is suggested", and (2)"Janniere does not disclose the use of oligonucleotide primer or any other means to introduce a D-loop at a selected location. Indeed, in the Janniere paper, the D loop is generated as a inherent result of the addition of the polymerase, and not as a separate step prior to the assembly of the replisome. There is no targeting of the D loop to a specific initiation site adjacent to a selected target region".

The arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, Janniere et al., (see page 526, right column, third paragraph) (Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-15, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
page(s) 17, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) NONE, filed with the demand.
and additional amendments:
Claim Page 16, filed with the letter of 13 December 2000.

This report has been drawn on the basis of the drawings,
page(s) 1, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) 1 and 2, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
showed that D loop structure was generated by DNA polymerase I in the initiation of pAMbeta1 replication. it is well known that the replisome is completed by polymerase III and is required for DNA replication(Devlin, Textbook of Biochemistry with clinical correlations, third Edition, see page 671, first paragraph). Therefore, the replisome formation in the presence of assembly proteins is a inherent property of the reference of Janniere et al., and will be considered as a separate step after D loop formation. Second, Janniere et al., clearly showed the use of oligonucleotide primer to introduce a D-loop (see page 533, left column, last paragraph). Third, in response to applicant's argument that the reference failed to show certain features of applicant's invention such as "no real world application of the observation of the replication intermediates is suggested" by Janniere et al., and "there is no targeting of the D loop to a specific initiation site adjacent to a selected target region" is suggested by Janniere et al., it is noted that the features upon which applicant relies above are not recited in the claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims.

Claims 1-5 lack an inventive step under PCT Article 33(3) as being obvious over Janniere et al., (Mol. Microbiology 23, 525-535, 1997)in view of Karet et al., (Anal. Biochem. 220, 384-390, 1994).

The teachings of Janniere et al., have been summarized previously, *supra*. This prior art meets the limitations of claims 1-4.

Janniere et al., do not disclose fluorescence labeled primer.

Karet et al., teach fluorescence labeled primer (page 384, abstract).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to have used performed the method for replication of a target region of a target DNA molecule as suggested by Janniere et al., using a fluorescence labeled primer. The prior art provided by Karet et al., would have motivated one having ordinary skill in the art to perform the method for replication of a target region of a target DNA molecule using a fluorescence-labeled primer. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to combine these prior arts together because all of prior art are known and are easy to use.

Claims 6-15 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the limitations of claims 6-15.